UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,428	10/24/2003	Claudia A. Robbins	10031294-1	2017

7590 03/15/2006

AGILENT TECHNOLOGIES, INC.
Legal Department, DL 429
Intellectual Property Administration
P. O. Box 7599
Loveland, CO 80537-0599

EXAMINER	
CROW, ROBERT THOMAS	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,428	ROBBINS ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 27 January 2006 is acknowledged. Claims 25-27 are withdrawn. Claims 1-24 are currently under prosecution.

Preliminary Amendments

1. The Preliminary Amendment filed 18 February 2004 containing the replacement sheet for Tables 3 & 4 of the Specification is acknowledged.

2. The Preliminary Amendment filed 26 November 2003 is acknowledged. In a telephone interview with Stephen Gaudet on 8 March 2006, the Examiner informed Applicant that the Preliminary Amendment had been improperly assigned to case 10/631,189. The Examiner was told the Preliminary Amendment belonged with the instant case. However, the Preliminary Amendment has not been properly filed. The Examiner suggests that the Preliminary Amendment be resubmitted with proper reference to the correct Application Number.

Information Disclosure Statement

The Information Disclosure Statement received 5 July 2005 is acknowledged. However, Documents DE 200 03 080 (dated 27 April 2000) and DE 197 46 874 (dated 29 April 1999) are not considered because English translations have not been provided.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-9 are indefinite in line 3 of claim 1, which recites the limitation "a tissue/cell lysate." ." It is unclear what the"/" symbol represents; e.g., if the symbol means "and" or "or."

2. Claims 1-9 are indefinite in line 4 of claim 1, which recites the limitation "the gDNA." It is suggested that "the gDNA" be replaced with "said genomic DNA." It is

also suggested that the term "the gDNA" in line 2 of claim 5 be replaced with "said genomic DNA." Claims 1-9 are also indefinite in line 5 of claim 1, which recites the limitation "the preparation" in line 5. There is insufficient antecedent basis for this limitation in the claim.

3. Claims 3 and 24 are indefinite in the recitations "BTS," "PVDF," "MMM," and "PVP" in line 2 of claim 3 and in lines 2-3 of claim 24 because they are acronyms, the meanings of which may change over time. It is suggested that each of the claims be amended to recite each of the polymers in each instance by their respective full names.

4. Claim 10 is indefinite in line 1, which recites the limitation "animal and plant tissues and/or cells." ." It is unclear what the"/" symbol represents; e.g., if the symbol means "and" or "or." Claim 10 is also indefinite the recitation "alike" at the end of the claim. It is unclear what is encompassed by the term "alike."

5. Claim 16 is indefinite in the recitation "Wash Buffer #1 and Wash Buffer#2" in line 2 of the claim. It is unclear what the reagents of each of the wash buffers are, or whether the buffers are the same or different. It is also unclear how "#1" and "#2" define or differentiate the buffers; e.g., composition, concentration of reagents, etc.

6. Claims 19-24 are indefinite in line 3 of claim 19, which recites the limitation "a tissue/cell lysate." It is unclear what the"/" symbol represents; e.g., if the symbol means "and" or "or."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6, 9, 10, 12, 14, 15, 16, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15 and pp. 7.26-7.29 (1989)).

Regarding claim 1, Sambrook et al teach a method of preparing RNA substantially free of genomic DNA, comprising the following steps: forming a tissue/cell lysate (page 7.12, step 1-page 7.14, step 11); removing essentially all of the gDNA (e.g., incubating with DNAse to digest all DNA; page 7.14, steps 13-15); forming a precipitate by adding an organic solvent to the preparation (e.g., ethanol; page 7.14, steps 15-18); contacting an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a membrane (e.g., paper filters

embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph).

Regarding claim 2, Sambrook et al teach the method of claim 1 wherein said membrane is a polymeric membrane (e.g., a paper membrane with poly(U) residues; page 7.29, paragraph 2).

Regarding claim 5, Sambrook et al teach the method of claim 1 wherein removing essentially all of the gDNA is accomplished by using a pre-filtration technique (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1).

Regarding claim 6, Sambrook et al teach the method of claim 1 wherein said lysate is formed employing a lysis buffer comprising a chaotropic agent (e.g., they lysis buffer has the detergent Nonidet P-40; page 7.12, step 2).

Regarding claim 9, Sambrook et al teach the method of claim 1 wherein said biological sample is animal cells (e.g., mammalian cells; page 7.12, line 1).

Regarding claim 10, Sambrook et al teach the method of claim 9 wherein said biological sample is mammalian cells (page 7.12, line 1), as encompassed by the phrase "and alike" at the end of claim 10.

Regarding claim 12, Sambrook et al teach the method of claim 1 wherein said precipitate comprises RNA essentially free of DNA (e.g., poly(A)+ RNA is selected; page 7.26, line 1).

Regarding claim 14, Sambrook et al teach the method of claim 1 wherein said organic solvent is ethanol (page 7.14, steps 13-15).

Regarding claim 15, Sambrook et al teach the method of claim 1 wherein said precipitate is washed following contact with the RNA isolation membrane column with a wash solution comprising an organic solvent (e.g., the RNA is stored in a TE buffer with ethanol prior to oligo(dT)-chromatography; page 7.14, step 18).

Regarding claim 16, Sambrook et al teach the method of claim 15 wherein said wash solution is Wash Buffer #2 (e.g., TE [pH 7.6] and ethanol [71% final concentration]; page 7.14, step 18).

Regarding claim 18, Sambrook et al teach the method of claim 16 wherein Wash Buffer #2 comprises from about 40% to about 90% ethanol and a buffering agent to maintain a pH from about 6 to about 9 (e.g., TE [pH 7.6] and ethanol [71% final concentration]; page 7.14, step 18).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-2, 4-10, 12-21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) in view of Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)).

Regarding claim 1, Colpan et al teach the method of preparing an RNA sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a filter material, wherein said filter material has at least one layer of glass (column 7, lines 30-36); forming a precipitate by adding an organic solvent to the prefiltration step (e.g., the column is washed with a buffer containing isopropanol

[Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17]);and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA (e.g., RNA is separated and purified; column 6, lines 7-8). While Colpan et al also teach use of the nucleic acid subsequent reactions (column 4, lines 15-21), Colpan et al are silent with respect to a second column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph). Sambrook et al also teach contact of said precipitate with an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a membrane (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Regarding claim 2, the method of claim 1 is discussed above. Sambrook et al teach the use of polymeric membranes (e.g., a paper membrane with poly(U) residues; page 7.29, paragraph 2).

Regarding claim 4, the method of claim 1 is discussed above. Colpan et al also teach fiber material having a particle retention ranging from about 0.1 microns to about 10 microns (e.g., the glass has a pore size of 1 micron; column 6, lines 60-67).

Regarding claim 5, the method of claim 1 is discussed above. Colpan et al also teach removing essentially all of the gDNA using a prefiltration technique (e.g., RNA is separated and purified by the column; column 6, lines 7-8).

Regarding claim 6, the method of claim 1 is discussed above. Colpan et al also teach chaotropic reagent in the preparation of the lysate (column 3, lines 1-8).

Regarding claim 7, the method of claim 6 is discussed above. Colpan et al also teach the chaotropic reagent guanidine hydrochloride (column 7, lines 60-67).

Regarding claim 8, the method of claim 7 is discussed above. Colpan et al also teach concentrations of chaotropic reagents ranging from about 0.5 M to about 5.0 M (Example 1, column 7, lines 64-66).

Regarding claim 9, the method of claim 1 is discussed above. Colpan et al also teach said biological sample are cells (column 5, lines 64-67).

Regarding claim 10, the method of claim 9 is discussed above. Colpan et al also teach said cells are blood (column 5, lines 64-67).

Regarding claim 12, the method of claim 9 is discussed above. Colpan et al also teach RNA essentially free of DNA (e.g., RNA is separated and purified by the column; column 6, lines 7-8).

Regarding claim 13, the method of claim 1 is discussed above. Colpan et al also teach lysis buffers comprising beta-mercaptoethanol (column 11, lines 62-67).

Regarding claim 14, the method of claim 1 is discussed above. Colpan et al also teach the organic solvent is isopropanol (e.g., the column is washed with a buffer containing isopropanol; Example 1, column 8, lines 4-10)

Regarding claim 15, the method of claim 1 is discussed above. Colpan et al also teach washing the precipitate with a wash solution comprising an organic solvent (e.g., the nucleic acids precipitated on the column [column 2, lines 12-17] are washed with 80%ethanol/water [column 8, lines 10-15]).

Regarding claim 16, the method of claim 15 is discussed above. Colpan et al also teach washing the precipitate with wash solution #2 (e.g., the nucleic acids precipitated

on the column [column 2, lines 12-17] are washed with TrisHCl (pH 7.5) and 30-80% ethanol [column 9, lines 33-38]).

Regarding claim 17, the method of claim 16 is discussed above. Colpan et al also teach Wash Buffer #1 comprising from about 0.2 to about 2M guanidine, from about 5 to about 25% ethanol, and a buffering agent to maintain a pH from about 6 to about 9 (e.g., Example 7, column 9, lines 10-33).

Regarding claim 18, the method of claim 16 is discussed above. Colpan et al also teach Wash Buffer #2 comprising about 40 to about 90% ethanol and a buffering agent to maintain a pH from about 6 to about 9 (e.g., TrisHCl (pH 7.5) and 30-80% ethanol; column 9, lines 33-38]).

Regarding claim 19, Colpan et al teach the method of preparing a sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a filter material, wherein said filter material has at least one layer of glass (column 7, lines 30-36); forming a precipitate by adding an organic solvent to the prefiltration step (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17]); and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA (e.g., plasmid

DNA, genomic DNA and RNA are separated and purified). While Colpan et al teach the use of a column to purify RNA (column 6, lines 10-12), Colpan et al are silent with respect to a second column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph). Sambrook et al also teach contact of said precipitate with an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a membrane (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification

would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al (page E10, first paragraph and page 7.26, first paragraph).

Regarding claim 20, the method of claim 19 is discussed above. Colpan et al also teach fiber material having a particle retention ranging from about 0.1 microns to about 10 microns (e.g., the glass has a pore size of 1 micron; column 6, lines 60-67).

Regarding claim 21, the method of claim 19 is discussed above. Colpan et al also teach fiber material having a thickness ranging from about 50 microns to about 2000 microns (column 6, lines 60-67).

Regarding claim 23, the method of claim 19 is discussed above. While Sambrook et al teach membranes in RNA isolation columns (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2), Sambrook et al do not teach the particle retention of said membranes. However, column membranes with particle retention ranging from about 0.1 to about 10 microns were well known in the art at the time the invention was claimed, as evidenced by the teaching of Colpan et al, wherein column membranes with particle retention in the micron range (e.g., membranes having pore sizes of about 5 microns; column 6, lines 44-51) are disclosed as having the added advantage of allowing lysate components to pass through without obstruction (column 6, lines 44-47).

2. Claims 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) and Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) as defined by the Aldrich Catalog (Aldrich Chemical Company, Milwaukee, WI, page T281 (1998/1999)).

Regarding claim 22, Colpan et al teach the method of preparing a sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a filter material, wherein said filter material has at least one layer of glass (column 7, lines 30-36); and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA (e.g., plasmid DNA, genomic DNA and RNA are separated and purified). While Colpan et al teach the use of a column to purify RNA (column 6, lines 10-12), Colpan et al are silent with respect to precipitation and a second column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page

E10, first paragraph. Sambrook et al also teach contact of said precipitate with an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a membrane (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al ([page E10, first paragraph and page 7.26, first paragraph]; i.e., the method of claim 19).

Colpan et al also teach the use of glass fibers (column 6, lines 60-67). Aldrich teaches glass fibers in 2 in diameter bundles that are 22 feet long, weighing 454 g (page T281, column 2, paragraph 1). A filter layer having a 2 in (5.08 cm) diameter has an area of 0.00203 m^2; therefore, a filter layer having a 2 in diameter and a length (i.e., the

thickness of the layer in a column) of 0.25 in has a specific weight of 212 g/m^2, thereby meeting the limitation of the claim. Further, it is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not posses characteristic relied on" (205 USPQ 594, second column, first full paragraph). In the instant case, Applicant must provide proof that the specific weight ranging from about 75 g/m^2 to about 300 g/m^2 as claimed represents a new and non-obvious property beyond what is commonly known in the art.

3. Claims 1, 3, 19, and 24 rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) and Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)) in view of Utermohlen (U.S. Patent No. 5,437,976, issued 1 August 1995).

Regarding claim 3, Colpan et al teach the method of preparing an RNA sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column

comprises a filter material, wherein said filter material has at least one layer of glass (column 7, lines 30-36); forming a precipitate by adding an organic solvent to the prefiltration step (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17]);and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA (e.g., RNA is separated and purified; column 6, lines 7-8). While Colpan et al also teach use of the nucleic acid subsequent reactions (column 4, lines 15-21), Colpan et al are silent with respect to a second column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph). Sambrook et al also teach contact of said precipitate with an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a membrane (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for

the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al ([page E10, first paragraph and page 7.26, first paragraph]; i.e., the method of claim 1). Colpan et al and Sambrook et al are silent with respect to nylon membranes.

However, Utermohlen et al teach mRNA affinity chromatography (Abstract, lines 3-5) using woven nylon matrices attached to poly(dT) (column 5, lines 52-59) having the added advantage of use as a priming matrix for cDNA synthesis (column 4, lines 8-11).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the RNA purification method as taught by Colpan et al and Sambrook et al with the nylon matrices as taught by Utermohlen with a reasonable expectation of success. The ordinary artisan would have made such a modification because the modification would have resulted in additional

use of the matrices as a priming matrix for cDNA synthesis as explicitly taught by Utermohlen (column 4, lines 8-11).

Regarding claim 24, Colpan et al teach the method of preparing a sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a filter material, wherein said filter material has at least one layer of glass (column 7, lines 30-36); and collecting the effluent from said column, wherein said effluent is substantially free of said genomic DNA (e.g., plasmid DNA, genomic DNA and RNA are separated and purified). While Colpan et al teach the use of a column to purify RNA (column 6, lines 10-12), Colpan et al are silent with respect to precipitation and a second column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph. Sambrook et al also teach contact of said precipitate with an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15,

paragraph ii), wherein said column comprises a membrane (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al ([page E10, first paragraph and page 7.26, first paragraph]; i.e., the method of claim 19). Colpan et al and Sambrook et al are silent with respect to nylon membranes.

However, Utermohlen et al teach mRNA affinity chromatography (Abstract, lines 3-5) using woven nylon matrices attached to poly(dT) (column 5, lines 52-59) having the added advantage of use as a priming matrix for cDNA synthesis (column 4, lines 8-11).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the RNA purification method as

taught by Colpan et al and Sambrook et al with the nylon matrices as taught by Utermohlen with a reasonable expectation of success. The ordinary artisan would have made such a modification because the modification would have resulted in additional use of the matrices as a priming matrix for cDNA synthesis as explicitly taught by Utermohlen (column 4, lines 8-11).

4. Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002) Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989))in view of Crossway et al (U.S. Patent No. 4,996,144, issued 26 February, 1991).

Regarding claim 11, Colpan et al teach the method of preparing an RNA sample substantially free of genomic DNA (e.g., a method for purification and separation of nucleic acid mixtures; Abstract, lines 1-2), comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), wherein said pre-filtration column comprises a filter material, wherein said filter material has at least one layer of glass (column 7, lines 30-36); forming a precipitate by adding an organic solvent to the prefiltration step (e.g., the column is washed with a buffer containing isopropanol [Example 1, column 8, lines 4-10] wherein the nucleic acids are precipitated on the surface of the glass fibers [column 2, lines 12-17]);and collecting the effluent from said

column, wherein said effluent is substantially free of said genomic DNA (e.g., RNA is separated and purified; column 6, lines 7-8). While Colpan et al also teach use of the nucleic acid subsequent reactions (column 4, lines 15-21), Colpan et al are silent with respect to a second column.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating nucleic acids (page E10, first paragraph). Sambrook et al also teach contact of said precipitate with an RNA isolation membrane column with said precipitate (e.g., performing oligo(dT) -cellulose type chromatography on the RNA; page 7.15, paragraph ii), wherein said column comprises a membrane (e.g., paper filters embedded with poly(U) residues; page 7.29, paragraph 2); and collecting said precipitate from said membrane, wherein said precipitate is substantially free of said genomic DNA (e.g., mRNAs are isolated; page 7.26, first paragraph) with the added benefit that the RNA isolation column allows for the essential step of preparing mRNA for use in construction of cDNA libraries (page 7.26, first paragraph).

It would therefore have been obvious to modify the method of preparing an RNA sample as taught by Colpan et al with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan

would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid and would also have fulfilled the essential step of preparing mRNA for use in construction of cDNA libraries as explicitly taught by Sambrook et al ([page E10, first paragraph and page 7.26, first paragraph]; i.e., the method of claim 1). While Colpan et al also teach DNA digestion (column 8, lines 61), neither Colpan et al not Sambrook et al teach digestion with DNAse after isolation of the precipitate.

However, Crossway et al teach a method of purification of nucleic acids (e.g., RNA; Abstract, lines 3-5) using digestion with DNAse with the added benefit of allowing differential detection of RNA only (column 5, lines 60-63).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the method of isolating a nucleic acid as taught by Colpan et al and Sambrook et al with the DNAse treatment as taught by Crossway et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in allowing differential detection of RNA only as explicitly taught by Crossway et al (column 5, lines 60-63).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/804,938 in view of Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002). Although the conflicting claims are not identical, both sets of claims are drawn to preparing an RNA sample, adding an organic solvent to the RNA sample, contacting said sample with an isolation column comprising a membrane, and eluting the RNA sample. The claims of the '938 application do not specify how the cRNA sample is prepared.

However, Colpan et al teach a method of purifying an RNA sample using a column comprising the following steps: forming a tissue/cell lysate from a biological sample (column 2, line 65); contacting a pre-filtration column with said lysate (column 7, lines 30-36), and collecting the effluent from said column, with the added benefit that said effluent is substantially free of said genomic DNA (e.g., RNA is separated and purified; column 6, lines 7-8).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to modify the claims of the '938 application with the prefiltration procedure as taught by Colpan et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in providing RNA that is separated and purified as explicitly taught by Colpan et al (column 6, lines 7-8).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2. Claims 19-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/914,920 in view of Sambrook et al (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, NY, pp. 7.12-7.15, pp. 7.26-7.29, and pp. E10-E.14 (1989)). Both sets of claims are drawn to methods form preparing an RNA sample comprising the steps of contacting a prefiltration column with a tissue

lysate, wherein said prefiltration column has a fiber material comprising at least one layer of glass or borosilicate fiber, contacting the RNA sample with an RNA isolation column, and eluting said RNA from said column. The claims of the '920 Application are silent with respect to precipitation with an organic solvent.

However, Sambrook et al teach a method of purifying RNA (e.g., poly(A)+ RNA; page 7.26, line 1) using RNA free of genomic DNA (page 7.12-page 7.15), wherein total cytoplasmic RNA is precipitated after removal of genomic DNA (e.g., gDNA is removed prior to chromatography; page 7.26, paragraph 1) with the added benefit that precipitation is a rapid and quantitative method for concentrating

It would therefore have been obvious to modify the method of preparing an RNA sample as claimed in the '920 Application with the precipitation and purification steps as taught by Sambrook et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in rapid and quantitative concentration of the nucleic acid as explicitly taught by Sambrook et al (page E10, first paragraph).

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert T. Crow
Examiner
Art Unit 1634